

- Sub C1
1. (Amended) A defective recombinant adenovirus comprising;
- the ITR sequences,
  - [a sequence permitting the] an encapsulation sequence, and
  - a heterologous DNA sequence,

wherein [and in which] the E1 gene has been rendered non-functional by deletion, and wherein the E2 or E4 genes have been rendered non-functional by deletion [and at least one of the E2, E4 and L1-L5 genes is non-functional].

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2. (Amended) An adenovirus according to claim 1, characterized in that [it is of human, animal or mixed origin] the adenovirus sequences are from a canine adenovirus.

Sub D1 Cont

3. (Twice Amended) An adenovirus according to claim 1 [2], characterized in that the [adenoviruses of human origin are chosen from those classified in group C] adenovirus sequences are from a human group C adenovirus.

B2 Sub D2

6. (Twice Amended) An adenovirus according to claim 1, characterized in that [it is devoid of] the late genes L1-L5 have been rendered non-functional by deletion.

Sub D3

9. (Amended) An adenovirus according to claim 1, characterized in that the [E1, E3 and E4 genes are deleted from its genome] E3 gene has been rendered non-functional by deletion.

Sub D4

10. (Amended) An adenovirus according to claim 9 [1], characterized in that the [E1, E3, L5 and E4 genes are deleted from its genome] L5 gene has been rendered non-functional by deletion.

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11. (Twice Amended) An adenovirus according to claim 1, characterized in that it comprises] further comprising a functional [gene] E3 gene under the control of a heterologous promoter.

12. (Twice Amended) An adenovirus according to claim 1, characterized in that the heterologous DNA sequence is [comprises one or more genes] selected from the group consisting of therapeutic genes and genes encoding antigenic peptides.

Sub D4

13. (Twice Amended) An adenovirus according to claim 12, characterized in that the heterologous DNA is a therapeutic gene which encodes a product selected from the group consisting of [is chosen from genes encoding] enzymes, blood derivatives, hormones, lymphokines, growth factors, neurotransmitters, precursors of neurotransmitters, synthetic enzymes, trophic factors, apolipoproteins, dystrophin, minidystrophin, tumor suppressor genes, and genes encoding factors involved in coagulation.

14. (Amended) An adenovirus according to claim 1 [12], characterized in that the heterologous DNA encodes an antisense sequence [therapeutic gene is an antisense gene or sequence whose expression in the target cell makes it possible to control the expression of genes or the transcription of cellular mRNAs].

15. (Amended) An adenovirus according to claim 12, characterized in that the heterologous DNA [gene] encodes an antigenic peptide capable of generating an immune response [in man] against microorganisms, tumors, or viruses.

16. (Amended) An adenovirus according to claim 15, characterized in that the gene encodes an antigenic peptide specific for a virus selected from the group consisting of the Epstein Barr virus, the HIV virus, the hepatitis B virus, and the pseudo-rabies virus [or alternatively specific for tumours].

17. (Twice Amended) An adenovirus according to claim 12, [characterized in that] wherein the heterologous DNA sequence [also comprises sequences permitting the expression of the one or more heterologous genes in the infected cell] further comprises a promoter.

18. (Twice Amended) An adenovirus according to claim 12, [characterized in that] wherein the heterologous DNA sequence [comprises, upstream of the therapeutic gene,] further comprises a signal sequence [directing the therapeutic product synthesized in the secretory pathways of the target cell].

19. (Twice Amended) A cell line [infectible by an adenovirus] comprising, integrated into its genome, [the functions necessary for the complementation of] the genes necessary to complement a defective recombinant adenovirus according to claim 1, wherein one of the complementing genes is under the control of an inducible promoter.

20. (Twice Amended) A cell line according to claim 19, characterized in that it comprises, in its genome, an [the] E1 gene and an E2 gene[s from an adenovirus] wherein the E2 gene is under the control of an inducible promoter.

22. (Twice Amended) A cell line according to claim 19, characterized in that it comprises, in its genome, an [the] E1 gene and an E4 gene[s from an adenovirus] wherein the E4 gene is under the control of an inducible promoter.

23. (Twice Amended) A cell line according to claim 19, further comprising a [characterized in that it additionally comprises the gene for the] glucocorticoid [glucocorticoid] receptor gene.

Sub 15 cont.  
B4  
cont.

24. (Twice Amended) A cell line according to claim 19, characterized in that it comprises E2 and E4 genes and the E2 and E4 genes are [placed] under the control of an inducible promoter.

25. (Amended) A cell line according to claim [24] 19, characterized in that the inducible promoter is the LTR promoter of MMTV.

26. (Twice Amended) A cell line according to claim 19, characterized in that it comprises a gene encoding the [E2 gene encodes the] 72 K protein of E2.

28. (Twice Amended) A [pharmaceutical] composition comprising a [at least one] defective recombinant adenovirus according to claim 1 and a pharmaceutically acceptable vehicle.

B5

29. (Twice Amended) A [pharmaceutical] composition[,] comprising a recombinant adenovirus according to claim 10 [5] and a pharmaceutically acceptable vehicle.

30. (Twice Amended) A [pharmaceutical] composition according to claim 28[, comprising a] wherein the vehicle is pharmaceutically acceptable for an injectable formulation.

Please add the following claims (claims 31-35):

--31. A defective recombinant adenovirus comprising;

- the ITR sequences,
- an encapsulation sequence, and
- a heterologous DNA sequence,

wherein the E3 and E4 genes have been rendered non-functional by deletion.

Sub C2  
B4  
Sub 16

32. An adenovirus according to claim 31, characterized in that the late genes L1-L5 have been rendered non-functional by deletion.

33. A cell line according to claim 19, characterized in that it comprises the open reading frames ORF6 and ORF6/7 of E4.

34. A defective recombinant adenovirus consisting essentially of;

- the ITR sequences,
  - an encapsulation sequence,
  - a heterologous DNA sequence, and
  - all or part of the E2 gene.
- Sub C3